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ASPERUGIN, A METABOLITE ASSOCIATED WITH ABNORMAL MORPHOLOGY OF ASPERGILLUS RUGULOSUS

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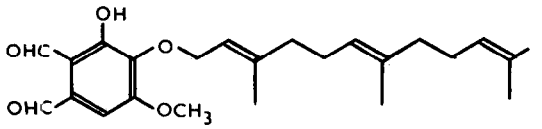
In the course of recombination experiments using mutants of Aspergillus rugulosus[1] it was found that all strains carrying a morphological marker "fluffy" produced a major phenolic compound which we have named asperugin. Related strains with wild-type morphology produced no asperugin; another apparently related compound was formed, instead, as the major phenolic metabolite.

Asperugin was isolated as a pale-yellow oil through counter-current distribution studies of the ether extract of the mycelium. Analytical data obtained using the phenol, its disemicarbazone and its condensation product with hydroxylamine (a monocyano, mono-oxime), together with evidence from n.m.r. and infrared spectroscopy, confirmed the presence of one methoxyl and two aldehydic carbonyl groups in the compound, $C_{24}H_{32}O_5$. Acid catalysed cleavage, using acid-washed silica gel, led to the formation of a crystalline phenol, $C_9H_8O_5$; this was identified as 3,4-dihydroxy-5-methoxyphthalaldehyde by reduction to 3,4-dihydroxy-5-methoxy-1,2-dimethylbenzene which was compared with synthetic material. The second product of cleavage was obtained more selectively by hydrogenolysis using sodium and methanol in liquid ammonia. It was identified as trans - trans - 2,6,10-trimethyldodeca-2,6,10-triene by reduction with hydrogen (3 moles) to farnesane, which was shown to be identical with authentic material by comparison of mass spectra. The occurrence of n.m.r. signals at τ = 8.34, 8.41, with equivalent integrals, confirmed the trans - trans - configuration of the farnesyl sidechain in

asperugin.[2] The point of attachment of this sidechain to the aromatic nucleus was suggested by the cleavage reactions and established as in the structure (I) by the presence of a doublet at τ = 5.40 (J = 7 c.p.s.); this is similar to the signal due to the related oxygen-linked methylene group in mycelianamide.[3,4] There was evidence in the infrared spectrum ($\nu_{max.}$ = 1635 cm.$^{-1}$) and the n.m.r. spectrum (τ = -2.62, singlet, integral for one proton, exchangeable with D_2O; attributed to -OH) for a strongly hydrogen-bonded hydroxyl-formyl system as in o-hydroxybenzaldehyde. This leads, unambiguously, to the assignment of the structure (I) to asperugin.



(I)

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